UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,007	10/19/2006	Dennis L. Panicali	701278	2230

45733 7590 11/10/2010

LEYDIG, VOIT & MAYER, LTD.
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
11/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,007	PANICALI ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-10,12,13,16-22 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,12,13,16-22 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/24/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/10 has been entered. Applicant's amendment and response also received on 9/24/10 has been entered. Claims 6, 11, 14-15, 23-39, and 41-43 are canceled. Claims 1-5, 7-10, 12-13, 16-22, and 40 are currently pending and under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Information Disclosure Statement

The information disclosure statement (IDS) filed on 9/24/10 meets the requirements of 37 CFR 1.97 and 1.98 and has been considered by the examiner. An initialed and signed copy of the 1449 is attached to this action.

Claim Objections

The objection to claims 4 and 17-22 are withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 112

The rejection of claims 17-22 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the amendments to these claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-5, 7-10, 12-13, 16, and 40 under 35 U.S.C. 103(a) as being unpatentable over WO 00/34494 (2000), hereafter referred to as Schlom et al., in view of WO 01/24832 (2001), hereafter referred to as Pecher, is maintained. Applicant's amendments to the claims and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the Office acknowledges that Schlom et al. does not teach a poxvirus vector encoding both MUC and CEA or a prime-boost protocol with two poxvirus vectors each encoding MUC and CEA and that Pecher et al. does not supply the missing teachings because Pecher does not teach a single vector encoding MUC and CEA.

In response, the applicant has only partially represented the teachings of Schlom et al. as set forth by the previous office actions. The rejection of record clearly states that Schlom et al. teaches the administration of more than one dose of recombinant poxvirus encoding a tumor antigen, such as MUC1 or CEA, or a prime and boost delivery method where a first vector is administered followed by a administration of a second vector, where the first and second vectors are different strains of poxvirus (Schlom et al., in particular page 39). The rejection of record

further states that Schlom et al. teaches that the poxvirus vector can encode **more than one** tumor associated antigen, and/or further encode a cytokine such as GM-CSF (Schlom et al., pages 5, 31-37). The only teaching missing from Schlom et al. is a specific teaching to choose MUC1 and CEA as the tumor associated antigens to express together in a recombinant poxvirus vector. Pecher was cited to supplement Schlom et al. by teaching the combined administration of vectors, including vaccinia virus vectors, encoding MUC1 and CEA to human patients for the treatment of tumors (Pecher et al. pages 4-6). Pecher was not cited for teaching a single vector encoding MUC and CEA. Schlom et al. already provides the teaching that the poxvirus can encode more than one tumor associated antigen, and Pecher was cited for providing the motivation to choose the combination of MUC1 and CEA to express in a single poxvirus vector as taught by Schlom et al. Likewise, Schlom et al. already provides the teachings for treating breast cancer. Therefore, it is reiterated that in view of the teachings of Schlom et al. to use poxvirus vectors encoding more than one target tumor associated antigen for the treatment of cancers including breast cancer, and the motivation provided by Pecher to co-administer vectors encoding MUC1 and CEA to treat human tumors, it would have been *prima facie* obvious to the skilled artisan at the time of filing to make and use a single poxvirus vector encoding MUC1, CEA, and TRICOM (B7, ICAM-1, and LFA-1) in the methods of treating cancer, such as breast cancer, taught by Schlom et al.. Further, based on the detailed guidance provided by Schlom et al. for making poxvirus vectors which encode multiple heterologous genes, and the successful demonstration by Schlom et al. that poxvirus encoding tumor antigens such as CEA and MUC1 can successfully prevent tumor growth, the skilled artisan at the time of filing would have had a

reasonable expectation of success in treating breast cancer using the methods of Schlom et al. as modified by Pecher et al.

The applicant further reiterates their argument that there are "unexpected benefits" to the present invention which would have been nonobvious at the time of filing. In addition to Gully et al., provided with a previous response, the applicant has now submitted additional references, including Tsang et al., Maden et al., Mohebtash et al., Palmowski et al., and Brody et al. which purportedly demonstrate that applicant's results would have been unexpected and surprising to the skilled artisan at the time of filing.

In response, the applicant is again reminded that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c). MPEP 716.02(g) further states: "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provided by 35 USC 25 and 18 U.S.C. 1001." Permitting a publication to substitute for expert testimony would circumvent the guarantees built into the statute. *Ex parte Gray*, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989). Publications may, however, be evidence of the facts in issue and should be considered to the extent that they are probative. With

this in mind, the pre- and post-filing publications cited in applicant's response have been considered.

The post-filing reference by Gulley et al. was provided with the previous response and addressed in detail in the previous office action which stated that while Gully et al. reports the practice of one embodiment of the method as claimed in human patients, there are no teachings in Gulley et al. that the co-expression of MUC1 and CEA resulted in "unexpected" or surprising results. In fact, while Gulley et al. on page 3060 suggests that vectors directed against multiple TAAs may evoke additive or synergistic immune responses, Gulley et al. does not report any additive or synergistic responses using the MUC1/CEA TRICOM vaccine. On the contrary, on page 3068, Gulley et al. remarks that a previous trial using a CEA TRICOM vaccine reported greater CEA specific T cell responses than those observed in the MUC1/CEA TRICOM trial. Therefore, Gulley et al. does not support applicant's argument for unexpected results.

The post-filing reference Tsang et al. provides preliminary *in vitro* test results for two different poxvirus vectors each comprising 5 transgenes encoding MUC1,CEA, B7, ICAM-1, and LFA-1 and demonstrates that dendritic cells infected with either poxvirus stimulates T cells against both the MUC1 and CEA antigens. Tsang et al. does not disclose any results from *in vivo* methods as claimed nor does Tsang et al. state that their *in vitro* results were surprising or unexpected. As such, Tsang et al. does not support applicant's argument for unexpected results.

Madan et al. is a brief report on an ongoing clinical trial comparing the effects of poxvirus vaccine comprising MUC1, CEA and TRICOM with or without concomitant docetaxel treatment. Madan et al. only reports on the safety of these treatments and provides no evidence or suggestion that any results obtained using poxvirus vaccine comprising MUC1, CEA and

TRICOM were "unexpected" or surprising. Likewise, Mohebtash et al. provides a brief update on the PANVAC (poxvirus comprising MUC1, CEA and TRICOM) with or without concomitant docetaxel clinical trials. While Mohebtash et al. states that both PANVAC alone or together with docetaxel show some clinical benefit to patients, this references provides no evidence or suggestion that any results obtained using poxvirus vaccine comprising MUC1, CEA and TRICOM were "unexpected" or surprising.

From the above analysis, none of the post-filing references provide any comparative data suggesting or demonstrating that the administration of a single poxvirus encoding MUC1 and CEA is unexpectedly more effective than the administration of two separate vectors, or that the skilled artisan would not have expected that the single vector encoding MUC1 and CEA would be capable of stimulating anti-tumor immune responses.

Finally, the references cited by the applicant which are part of the prior art published before applicant's filing date do not support applicant's argument that skilled artisan at the time of filing would not have expected that administration of a single poxvirus encoding MUC1 and CEA would stimulate the immune system against the CEA and MUC1 antigens. Brody et al. is a 1972 report about the phenomenon of antigen competition when administering protein antigen fragments. Brody et al. is silent as to immunization with MUC1 or CEA or the use of poxvirus to administer either or both of these antigens. Palmowski et al., a more recent article, discusses ways to improve the immune response to multiple antigens in a prime-boost strategy. However, Palmowski et al. clearly shows that the initial administration of a single vector encoding more than CTL peptide epitope was clearly effective in stimulating CTL against all of the encoded peptide epitopes. While Palmowski et al. showed that boosting with the same vector results in a

higher immune response to some epitopes versus other epitopes contained within the vector, this result does not change the fact that the skilled artisan would have had a reasonable expectation that one or more administration of the same or two different poxvirus vectors encoding both MUC1 and CEA would be capable of inducing an immune response against a breast tumor expressing these antigens. The applicant is reminded that the claims as written contain no limitations as the specific characteristics of the immune response generated, and neither the working example provided nor the post-filing references discussed above demonstrate that practice of the method as claimed produces an immune response against the poxvirus encoded MUC1 or CEA that was unexpected or surprising.

Thus, for the reasons set forth above, the rejection of record stands.

Applicant's amendments to claims 17-22 have necessitated the following rejection.

Claims 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/34494 (2000), hereafter referred to as Schlom et al., in view of WO 01/24832 (2001), hereafter referred to as Pecher, as applied to claims 1-5, 7-10, 12-13, 16, and 40 above, and further in view of Grosenbach et al. (2001) Cancer Research, Vol. 61, 4497-4505.

The teachings of Schlom et al. in view of Pecher are set forth above and in further detail in previous office actions, and provide both the teachings and motivation to make and use a single poxvirus vector encoding MUC1, CEA, and TRICOM (B7, ICAM-1, and LFA-1) in the methods of treating cancer, such as breast cancer, taught by Schlom et al.

However, although Schlom et al. teaches the administration of more than one dose of a recombinant virus, or a prime and boost delivery method where a first vector is administered followed by a administration of a second vector, where the first and second vectors are different strains of poxvirus, Schlom et al. does not specifically teach where 1-3 doses of an orthopox, such as vaccinia, NYVAC, or MVA, and multiple administration of an avipox are administered to the patient. Grosenbach et al. supplements Schlom et al. and Pecher by teaching a vaccine strategy for administering poxvirus encoding tumor associated antigen and TRICOM that synergistically amplifies tumor antigen specific immune responses. Specifically, Grosenbach et al. teaches that a prime/boost strategy where a orthopox vaccinia virus encoding CEA and TRICOM is administered once followed by three boosts of a fowlpox encoding CEA and TRICOM substantially enhances tumor antigen specific immune responses (Grosenbach et al., pages 4501-4503).

Therefore, in view of the teachings of Schlom et al. to administer different strains of poxvirus encoding more than one tumor associated antigen, such as MUC or CEA, and TRICOM in a prime boost strategy, the motivation provided by Pecher to co-express MUC and CEA for tumor therapy, and the particular motivation provided by Grosenbach et al. to prime using one dose of vaccinia encoding tumor antigen and TRICOM and boost with multiple doses of a fowlpox encoding tumor antigen and TRICOM, it would have been *prima facie* obvious to the skilled artisan at the time of filing to administer a priming dose of an orthopox such as vaccinia, or other well known modified vaccinia such as NYVAC or MVA as taught by Schlom, encoding MUC1, CEA, and TRICOM followed by boosting with multiple doses of fowlpox encoding MUC1, CEA, and TRICOM to a patient at risk for or having a breast tumor with a reasonable

expectation of success in preventing or delaying tumor growth. It is further noted that while Schlom et al. generally teaches repeat administrations of poxvirus and does not identify any particular interval between boosts of poxvirus, and Grosenbach et al. only specifically discloses repeat administrations of fowlpox at 1 or 2 week intervals, the normal desire of the artisan to improve upon what is already known would render the administration of boosts at for example 3 week intervals obvious. The applicant is reminded that "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for

electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633